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REVIEW PAPER

Endoscopic versus open approach in craniosynostosis repair: a systematic review and meta-analysis of perioperative outcomes

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Abstract

Introduction Surgery for craniosynostosis remains a crucial element in successful management. Intervention by both endoscopic and open approaches has been proven effective. Given the differences in timing and indications for these procedures, differences in perioperative outcomes have yet to be thoroughly compared between the two approaches. The aim of the systematic review and meta-analysis was to assess the available evidence of perioperative outcomes between the two approaches in order to better influence the management paradigm of craniosynostosis.

Methods We followed recommended PRISMA guidelines for systematic reviews. Seven electronic databases were searched to identify all potentially relevant studies published from inception to February 2018 which were then screened against a set of selection criteria. Data were extracted and analyzed using meta-analysis of proportions.

Results Twelve studies satisfied all the selection criteria to be included, which described a pooled cohort involving 2064 craniosynostosis patients, with 965 (47%) and 1099 (53%) patients undergoing surgery by endoscopic and open approaches respectively. When compared to the open approach, it was found that the endoscopic approach conferred statistically significant reductions in blood loss (MD = 162.4 mL), operative time (MD = 112.38 min), length of stay (MD = 2.56 days), and rates of perioperative complications (OR = 0.58), reoperation (OR = 0.37) and transfusion (OR = 0.09), where all $p < 0.001$.

Conclusion Both endoscopic and open approaches for the surgical management of craniosynostosis are viable considerations. The endoscopic approach confers a significant reduction in operative and postoperative morbidity when compared to the open approach. Given that specific indications for either approach should be considered when managing a patient, the difference in perioperative outcomes remain an important element of this paradigm. Future studies will validate the findings of this study and consider long-term outcomes, which will all contribute to rigor of craniosynostosis management.

Keywords Craniosynostosis · Open · Minimally invasive · Endoscopic · Microscopic · Sagittal · Metopic · Complications

Abbreviations

GRADE	Grading of Recommendations Assessment Development and Evaluation
NOS	Newcastle-Ottawa Scale
OR	Odds ratio
RR	Relative risk
MD	Mean difference
SMD	Standardized mean difference

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Introduction

Craniosynostosis, defined as premature closure of a cranial suture, occurs in 1:2000 to 1:2500 living births [2, 4]. Surgical correction is often warranted to achieve a normal head shape and also to prevent risks such as neurocognitive sequelae posed by increased intracranial pressure. Diverse spectrums of surgical techniques have evolved with time to treat craniosynostosis. Strip craniectomy was initially introduced by Lannelongue [18] and Lane [17] in the 1890s with the aim of preserving intellectual function but better cosmesis was found with open calvarial vault reconstruction [24]. More recently, there has been a renewed interest in craniectomy procedures due to availability of minimally invasive endoscopic procedures characterized by lower blood loss, operative time, and length of stay with acceptable long-term anthropometric outcomes since it is performed early in life [5, 8, 10, 26]. Postoperatively, molding helmet therapy is typically required to obtain good long-term cosmetic results with endoscopic treatment [26].

Many series have characterized perioperative outcomes following endoscopic and open repair of craniosynostosis [26]. A consolidated review of complications and reoperations following either technique is lacking in the literature. Also, no large-scale literature review has focused on evaluating these reports to assess quality of evidence comparing the two approaches. We aimed to perform a systematic review and meta-analysis comparing endoscopic and open craniosynostosis correction primarily with the objective of characterizing perioperative outcomes such as blood loss, operative time, length of stay, complication, reoperation, and transfusion rates following the procedure and provide recommendations using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [3].

Methods

Literature search strategy

Our systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [21]. The literature search strategy was designed around the PICO format—Is there a difference in surgical outcomes (outcome) between patients undergoing minimally invasive surgery (population of interest) and patients undergoing open surgery (comparison) following craniosynostosis correction (intervention)? Electronic searches were performed using Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, and Database of Abstracts of Review of Effectiveness from their dates of inception to February 2018 by two independent reviewers (A.G. and V.M.L.). We combined the search terms "craniosynostosis," "minimally invasive," "endoscopic," "open," "strip craniectomy," "calvarial reconstruction," "sagittal," and "metopic" as either keywords or MeSH terms. In addition, we reviewed the list of references from retrieved articles for identification of potentially relevant studies.

Selection criteria

The inclusion criteria used to screen all identified articles were the following: (1) original studies in human subjects, written in the English language; (2) distinct discernible cohorts of patients undergoing minimally invasive and open craniosynostosis repair in the same study; and (3) greater than 10 patients in each of the two groups. Studies were excluded if (a) lacking direct comparison between minimally invasive and open procedures, (b) no relevant outcomes were reported; and (c) among duplicate studies by the same institution with an accumulated number of patients or extended follow-up, only the most complete and updated reports were selected for quantitative synthesis. Reviews and editorials were also excluded. To minimize methodological heterogeneity, we only included studies which reported use of endoscopic-assisted minimally invasive procedures.

Data extraction and critical appraisal

All data were extracted from article texts, tables, and figures with any estimates made based on the presented data and figures. Two investigators (A.G. and V.M.L.) independently reviewed each included article, any discrepancy resolved by discussion to reach consensus. Primary outcomes of interest consisted of (a) reoperations, (b) perioperative complications (both intraoperative and postoperative complications), and (c) transfusion rates while secondary outcomes included perioperative parameters such as (a) estimated blood loss (EBL), (b) operative time, and (c) length of stay (LOS).

Risk of bias in each study was evaluated using the Newcastle-Ottawa Scale (NOS) [6]. Overall confidence in the estimates for each outcome was assessed based on the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) Working Group system for limitations in study design, evidence directness, consistency, precision of results, and publication bias [3]. The GRADEpro Guideline Development Tool (GDT) was employed to generate a Summary of Findings (SoF) table (https://gradepro.org/). In case a large effect size (defined as RR > 2 for categorical outcomes and standardized mean difference > 0.8 for continuous outcomes) was observed, strength of evidence was upgraded by one level.

Statistical analysis

Odds ratios (OR) and mean differences (MD) were used as summary statistics for dichotomous and continuous outcomes, respectively. Meta-analyses for all outcomes were presented as forest plots with summary statistical estimates, 95% confidence intervals, and relative weights represented by the middle of the square, the horizontal line, and the relative size of the square, respectively. For the overall summary statistic, the mean and 95% confidence interval were represented by the middle and width of the diamond, respectively. The I^2 statistic was used to estimate heterogeneity across studies, with values greater than 50% considered as substantial heterogeneity. It can be calculated as $I^2 = 100\% \times (Q - df)/Q$, with Q defined as Cochrane's heterogeneity statistics and df defined as degrees of freedom. In the present meta-analysis, we used a *random-effects model* in order to take into account the methodological variation across studies. *Leave-one out sensitivity analysis* was performed when cohort size bias was suspected. Each study was sequentially removed, and the overall trend reassessed for any significant change. All p values were two-sided. All statistical analyses were conducted using Review Manager version 5.3.3 (Cochrane Collaboration, Software Update, Oxford, UK).

Results

Study characteristics

Our search yielded a total of 500 articles following which 278 were selected for screening following removal of duplicates and non-English reports. Following screening, 35 were selected for full-text evaluation and 12 studies [1, 2, 5, 8, 10, 16, 23, 26, 27, 29–31] were included in the final qualitative and quantitative synthesis (Fig. 1). All included studies were either retrospective ($n = 10$) or prospective ($n = 2$) observational in design. Most of the studies were from the USA ($n = 9$) while others were published from the Netherlands ($n = 2$) and Canada ($n = 1$). Table 1 summarizes characteristics of included studies.

Cohort description

A total of 2064 patients were included with 965 patients undergoing minimally invasive procedures. Sex distribution was reported in nine studies ($n = 1537$), out of 68% ($n = 1055$) were males. A majority of the studies ($n = 5$) focused on sagittal craniosynostosis only while the rest reported outcomes for metopic ($n = 2$), lambdoid ($n = 1$), or multiple different synostotic cranial sutures ($n = 4$). Eight studies ($n = 1673$) compared endoscopic procedures to open calvarial vault reconstruction while one study ($n = 35$) used strip craniectomy and another ($n = 300$) reported both calvarial vault reconstruction and open strip craniectomy as comparison. Two studies ($n = 356$) did not specify the type of open craniosynostosis surgery performed. Endoscopic procedures were mostly performed in case of early presentation (age < 6 months) with mean age of cohort ranging between 2.9 and 5.3 months while the mean age for open procedures ranged between 5 and 29.5 months with only study (Thompson et al. [27]) reporting a cohort of patients < 6 months of age (mean age 5 months) undergoing open procedures (after propensity score matching). Table 2 summarizes cohort characteristics.

Primary outcomes

Perioperative complications

A significantly lower complication rate was found with endoscopic procedures than open repair based on six studies ($n = 1872$). ($OR = 0.58$, $CI = 0.44–0.75$, $p < 0.001$, $I^2 = 0\%$) (Fig. 2a).

Reoperations

Compared to open surgery, endoscopic correction was associated with a significantly lower reoperation rate based on three studies ($n = 815$, $OR = 0.37$, $CI = 0.18–0.75$, $p = 0.006$, $I^2 = 0\%$) (Fig. 2b). A total of 12 reoperations were performed in the endoscopic group for cosmetic reasons ($n = 6$), bone defects ($n = 4$), CSF leak ($n = 1$), and recurrent synostosis ($n = 1$). In the open surgery group, a total of 38 revisions were performed for cosmetic reasons ($n = 9$), bone defects ($n = 8$), recurrent synostosis ($n = 8$), wound infection ($n = 4$), implant removal ($n = 3$), raised ICP ($n = 2$), and hematomas ($n = 2$).

Transfusion rate

Based on seven studies ($n = 1600$), endoscopic correction necessitated a significantly lesser transfusion requirement as reflected in the lower transfusion incidence as compared to open procedures ($OR = 0.09$, $CI = 0.03–0.26$, $p < 0.001$, $I^2 = 84\%$) (Fig. 2c).

Secondary outcomes

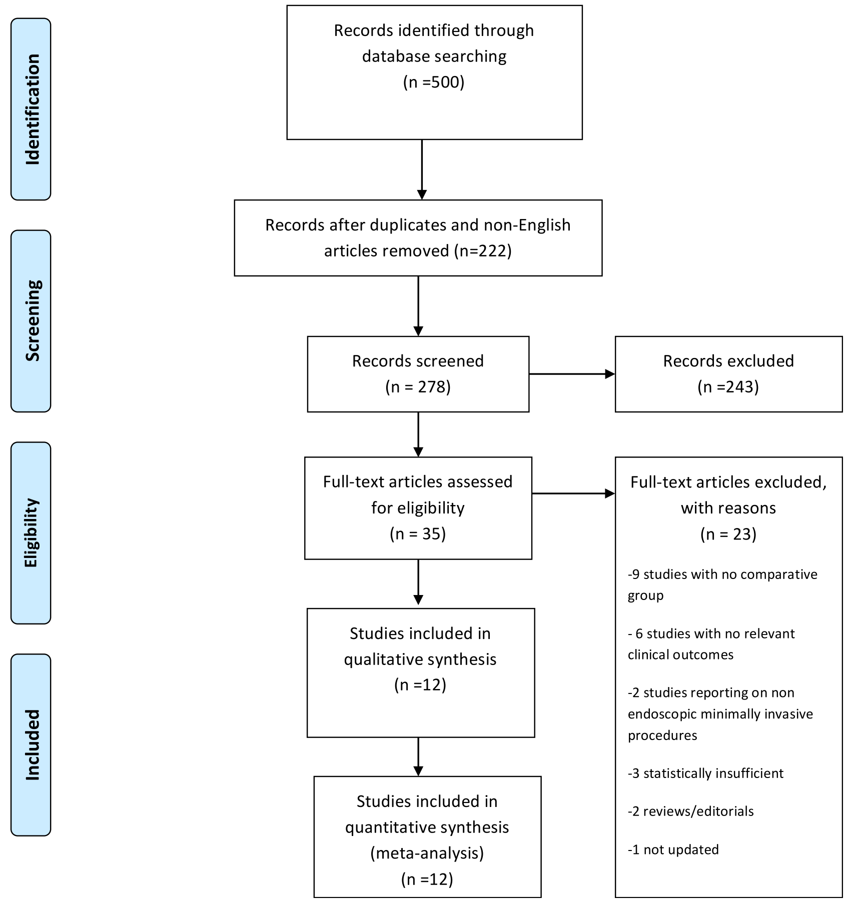
Estimated blood loss (mL)

Blood loss was reported by eight studies ($n = 1041$), significantly lower surgical blood loss was found with endoscopic surgery than open repair ($MD = 162.40$, $CI = 79.28–245.51$, $p < 0.001$, $I^2 = 0\%$) (Fig. 3a).

Operative time (minutes)

Based on nine studies ($n = 1812$), operative time was considerably shorter with endoscopic repair than open surgery ($MD = 112.38$, $CI = 88.64–136.12$, $p < 0.001$, $I^2 = 97\%$) (Fig. 3b).

Fig. 1 PRISMA search strategy



Length of stay (days)

Analysis of nine studies ($n = 1837$) reporting length of stay (LOS) revealed a significantly shorter length of hospital stay with endoscopic procedures compared to open surgery (MD = 2.56, CI = 1.89–3.23, $p < 0.001$, $I^2 = 97\%$) (Fig. 3c).

Quality assessment

Study quality was evaluated using the Newcastle-Ottawa Scale (NOS) [6]. A medium to high quality was observed for all studies included in this meta-analysis [Supplemental table 1]. Strength of evidence for all outcomes evaluated using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach was very low. (Table 3). With the exception of complications, strength of evidence for all outcomes was upgraded by one level because of a large effect size (defined as RR > 2 for categorical outcomes and SMD > 0.8 for continuous outcomes).

Discussion

Endoscopic-assisted craniosynostosis surgery was introduced in the 1990s by Jimenez and Barone [12–15, 19]. It remains a relatively newer technique with limited experience reported in the literature. The main goal is to minimize perioperative morbidity while achieving similar functional and cosmetic outcomes.

In the present systematic review and meta-analysis, we found superior perioperative performance of minimally invasive endoscopic surgery compared to open surgery. Pooled estimates revealed a lower complication rate following endoscopic procedures. In their retrospective study of 35 patients, van Nunen et al. found that endoscopic surgery simplified anesthesia practice on account of anticipation of increased hemodynamic stability and thereby, reducing the need for invasive monitoring by arterial cannulation [29]. Tobias et al. noted that a lower incidence of venous air embolism was observed with endoscopic surgery primarily attributable to a lower blood loss leading to a lower propensity to have non-compressible veins exposed to air [28]. Intraoperative

Table 1 Baseline study characteristics

Author	Year	Country	Retrospective/ prospective	Observational/ RCT	Number of institutions	Craniosynostosis type
Arts	2018	The Netherlands	Retrospective	Observational	1	All sutures
Chan	2013	USA	Retrospective	Observational	2	Coronal, metopic, sagittal
Han	2016	USA	Retrospective	Observational	1	All sutures
Thompson	2017	USA	Retrospective	Observational	1	All sutures
Garber	2017	Canada	Retrospective	Observational	1	Sagittal
Keshavarzi	2009	USA	Retrospective	Observational	1	Metopic
Nguyen	2014	USA	Retrospective	Observational	1	Metopic
Van Nunen	2016	The Netherlands	Retrospective	Observational	1	Sagittal
Vogel	2014	USA	Retrospective	Observational	1	Sagittal
Zubovic	2015	USA	Prospective	Observational	1	Lambdoid
Abbott	2012	USA	Retrospective	Observational	1	Sagittal
Shah	2011	USA	Prospective	Observational	1	Sagittal

durotomies have also been found to be lower with endoscopic approaches [2, 5, 10]. Also, of interest to note was the significantly lower reoperation and blood transfusion rate. These results have been shown to be consistent across both nonsyndromic and syndromic cases of craniosynostosis [10]. Most studies support a significantly lower intraoperative complication rate while a modest benefit has been noted in terms of incidence of postoperative complications [10, 26]. Several studies have demonstrated lower hospital costs with endoscopic approaches despite the costs incurred due to postoperative orthotic therapy [5, 8, 11, 30]. This might be indirectly due to a lower length of hospital stay and lesser transfusion requirements as found in this study. The lower perioperative morbidity also avoids the costs associated with stay in an intensive care unit [30]. According to the multicenter evaluation by Thompson et al., a majority of participating centers (60%) did not practice intensive care admissions after endoscopic surgery [27].

While this review focuses primarily on perioperative safety and efficacy, long-term anthropometric outcomes with endoscopic-assisted surgery are also said to be equivalent to open calvarial reconstruction [7, 20, 23, 26]. This is an important consideration in determining the optimal approach in a craniosynostosis patient at presentation. In their retrospective review of 89 patients with sagittal craniosynostosis, Shah et al. [26] found mean cephalic index at the last follow-up to be equivalent between the two groups. However, significantly longer follow-up was noted in the open group compared to the endoscopic group (24 vs 13 months). In another review of 46 patients with sagittal craniosynostosis by Le et al., no significant differences were found in mean cranial index at 24 months between endoscopic and open surgery patients [20]. Surgical technique was not determined to be a significant factor in postrepair anthropometric outcome. Literature on metopic craniosynostosis is largely insufficient to suggest equivalence or non-inferiority of the endoscopic technique over open repair; however, emerging results are encouraging. Nguyen et al. demonstrated similar postoperative measurements following endoscopic and open repair in a series of 28 patients with nonsyndromic metopic craniosynostosis despite worse hypertelorism in the endoscopic group ($n = 13$) at baseline [23].

Compared to open procedures, endoscopic suturectomies were performed at a significantly younger age with most authors preferring the procedure only at an age of presentation less than 6 months [1, 2, 5, 7–10, 16, 20, 23, 26, 27, 30]. While surgery at a younger age could potentially be associated with a higher complication rate, the lower blood loss and surgical time with a minimally invasive procedure seemed to compensate for the morbidity of an operative intervention in a young patient. According to available anthropometric evaluations, age of repair is a significant predictor of improvement in cranial measurements [20, 23]. Success of endoscopic correction is often attributed to the younger age of suturectomy, allowing cranial remodeling with brain development [23, 26]. The younger age of intervention warrants postoperative helmet therapy to "mold" the steep calvarial bone growth. In contrast, since open procedures are performed at an older age, postoperative molding therapy is deferred to due to decline in the rate of bone development.

It is important to note, that a successful long-term outcome with endoscopic repair is critically dependent on postoperative molding with helmet (orthotic) therapy to augment cranial index [23, 26], although its exact recommended duration

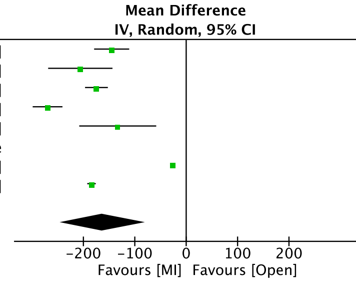
Table 2 Cohort size and description

Author	Surgical technique-MIS	Surgical technique—open	Total cohort (*n*)			MIS			Open		
			Size (*n*)	Male (*n*)	Mean age (month)	Size (*n*)	Male (*n*)	Mean age (month)	Size (*n*)	Male (*n*)	Mean age (month)
Arts	Endoscopically assisted craniosynostosis surgery	Open cranial vault reconstruction surgery	187	–	6.76 ± 3.81	121	–	3.9 ± 1.1	66	–	12 ± 8.8
Chan	Endoscope-assisted strip craniectomy	Open cranial vault	57	26 (45.6%)	–	36	18 (50%)	4.74 (1.93–9.1)	21	8 (38%)	10.6 (5.33–21.23)**
Han	Endoscopic craniosynostosis surgery	Open craniosynostosis surgery	328	–	12.3 (12.4)	150	–	3.43 (1.21)	178	–	17.2 (19.0)
Thompson	Endoscopic craniectomy	Anterior and/or posterior cranial vault reconstruction, modified-Pi procedure, or strip craniectomy	933	621 (66.6%)	–	311	216 (70%)	3 (2–4)*	622	405 (65%)	5 (3–6)*
Garber	Endoscopic strip craniectomy	Total cranial vault reconstruction (100), open sagittal strip craniectomy (100)	300	226 (75.3)	4.74 (2.3)	100	75 (75)	2.9 (0.76)	200	151 (75.5)	5.7 (3.1)
Keshavarzi	Endoscopic	Fronto-orbital advancement with calvarial reconstruction	33	25 (75.7)	17.57	16	14 (87.5)	4.9	17	11 (64.7)	29.5
Nguyen	Endoscopic	Open	28	70%	6.62 (1.15)	13	70%	3.3 ± 0.4	15	70%	9.5 ± 1.8
van Nunen	Minimally invasive strip craniectomy	Open extended strip craniectomy	35	27 (77.1%)	–	20	16 (80.0)	21.2 (18.9–23.8)[ƀ]	15	11 (73.3)	34.4 (23.7–50.4)[ƀ]
Vogel	Endoscope-assisted craniectomy	Open cranial vault modeling	42	28 (66.7%)	4.95 (0.3)	21	12 (57.1%)	3.1 ± 0.2	21	16 (76.2%)	6.8 ± 0.4
Zubovic	Endoscopic-assisted strip suturectomy	Posterior cranial vault remodeling	12	–	–	4	–	5.1	8	–	10.8
Abbott	Endoscopically assisted suturectomy	Open cranial vault remodeling	20	13 (65%)	–	10	7 (70%)	2.3 (0.4–3.7)	10	6 (60%)	10.9 (5.1–38.9
Shah	Endoscopic	Open calvarial vault reconstruction	89	69 (70.8%)	4.83	47	32 (68%)	3.6	42	31 (74%)	6.8

*Median and range is reported. **Mean and range is reported. ƀ Age reported in weeks

Study or Subgroup	Minimally invasive Mean	SD	Total	Open Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Arts 2018	35	28	121	180	140	66	14.4%	−145.00 [−179.14, −110.86]
Chan 2013	74	122.5	36	280	112.5	21	13.6%	−206.00 [−268.58, −143.42]
Garber 2017	35	32	83	209.6	147.2	187	14.6%	−174.60 [−196.79, −152.41]
Han 2016	36.5	27.7	150	306.2	194.9	178	14.5%	−269.70 [−298.67, −240.73]
Keshavarzi 2009	56.8	37	16	190	152.9	17	13.2%	−133.20 [−208.11, −58.29]
Shah 2011	29	0	47	218	152.9	42		Not estimable
van Nunen 2016	3.8	3.03	20	29.7	9.26	15	14.8%	−25.90 [−30.77, −21.03]
Vogel 2014	28.9	3.5	21	213.1	19.1	21	14.8%	−184.20 [−192.51, −175.89]
Total (95% CI)			**494**			**547**	**100.0%**	**−162.40 [−245.51, −79.28]**

Heterogeneity: $Tau^2 = 12158.26$; $Chi^2 = 1340.50$, df = 6 ($P < 0.00001$); $I^2 = 100\%$
Test for overall effect: Z = 3.83 (P = 0.0001)



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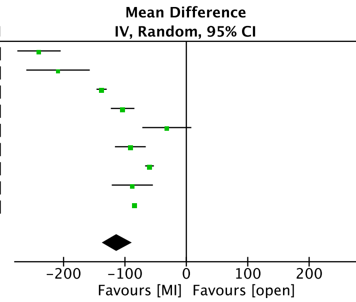
Study or Subgroup	Minimally invasive Mean	SD	Total	Open Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Abbott 2012	120	22.2	10	360	52.5	10	10.1%	−240.00 [−275.33, −204.67]
Chan 2013	133	42.25	36	342	116.5	21	8.0%	−209.00 [−260.70, −157.30]
Garber 2017	68	13	78	206	56	197	12.8%	−138.00 [−146.34, −129.66]
Han 2016	75.2	29.4	150	179	126.6	178	12.0%	−103.80 [−122.98, −84.62]
Keshavarzi 2009	100.8	31	16	132.6	77.7	17	9.5%	−31.80 [−71.74, 8.14]
Shah 2011	87.8	31	47	179	77.7	42	11.4%	−91.20 [−116.31, −66.09]
Thompson 2017	70	37	311	130	74	622	12.9%	−60.00 [−67.12, −52.88]
van Nunen 2016	90	34	20	178	59.25	15	10.3%	−88.00 [−121.48, −54.52]
Vogel 2014	81.1	3.2	21	165.8	5.7	21	13.0%	−84.70 [−87.50, −81.90]
Total (95% CI)			**689**			**1123**	**100.0%**	**−112.38 [−136.12, −88.64]**

Heterogeneity: $Tau^2 = 1127.70$; $Chi^2 = 305.25$, df = 8 ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: Z = 9.28 (P < 0.00001)



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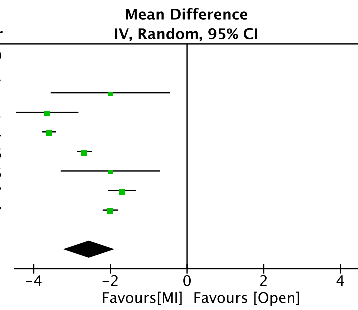
Study or Subgroup	Minimally invasive Mean	SD	Total	Open Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Keshavarzi 2009	2.46	1.18	16	2.76	0	17		Not estimable	2009
Shah 2011	1.2	1.18	47	3.9	0	42		Not estimable	2011
Abbott 2012	1	1.18	10	3	2.22	10	8.9%	−2.00 [−3.56, −0.44]	2012
Chan 2013	1.25	1	36	4.9	1.75	21	13.7%	−3.65 [−4.47, −2.83]	2013
Vogel 2014	1.1	0.1	21	4.7	0.4	21	16.9%	−3.60 [−3.78, −3.42]	2014
Han 2016	1.12	0.32	150	3.8	1.3	178	16.9%	−2.68 [−2.88, −2.48]	2016
van Nunen 2016	4	1.48	20	6	2.22	15	10.4%	−2.00 [−3.30, −0.70]	2016
Garber 2017	1.8	1.4	100	3.5	1.75	200	16.3%	−1.70 [−2.07, −1.33]	2017
Thompson 2017	2	1.48	311	4	1.48	622	16.9%	−2.00 [−2.20, −1.80]	2017
Total (95% CI)			**711**			**1126**	**100.0%**	**−2.56 [−3.23, −1.89]**	

Heterogeneity: $Tau^2 = 0.68$; $Chi^2 = 181.39$, df = 6 ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: Z = 7.49 (P < 0.00001)



C

Fig. 2 Forest plots comparing **a** estimated blood loss **b** operative time, and **c** length of stay between open and minimally invasive craniosynostosis repair. MI minimally invasive

remains under investigation [13, 22, 25]. The addition of orthotic use has not been demonstrated to significantly increase costs [5, 8, 30]. Although complications related to orthotic therapy (such as alopecia) have been said to be insignificant [26], compliance with the regimen remains a significant challenge to be observed. Therefore, caregiver socioeconomic characteristics that determine compliance need to be taken into consideration during preoperative counseling and individually tailored decision-making.

Limitations

This review was marked by several limitations. First, the impact of age as a confounding factor to determine outcomes between the two groups could not be assessed. However, randomizing patients into endoscopic or open groups would not be ethically possible given the different recommended ages for each procedure. In such a scenario, propensity-matched comparisons could be useful. Only one study in our review [27] employed propensity matching. Second, no prospective randomized comparisons were available with most included studies being single-institutional retrospective reviews, thereby, lowering study quality and strength of evidence, as shown by our overall GRADE estimates. However, large effect sizes were observed for all analyzed outcomes with the exception of complications. Third, the significantly shorter duration of follow-up in patients undergoing endoscopic repair in some studies could have been an important confounding factor for the lower reoperation rate seen in these patients [8, 10]. Fourth, due to limited availability within current literature, long-term anthropometric outcomes could not be quantitatively compared between the two types of procedures. Fifth, the difference in outcomes between the two techniques could not be stratified by the syndromic or nonsyndromic nature of the disease. Sixth, subgroup comparisons could not be performed to account for variations in technique of open repair–total

Study or Subgroup	Minimally invasive Events	Minimally invasive Total	Open Events	Open Total	Weight	Odds Ratio M-H, Random, 95% CI
Arts 2018	9	121	9	66	7.0%	0.51 [0.19, 1.35]
Garber 2017	0	100	3	200	0.8%	0.28 [0.01, 5.49]
Han 2016	13	150	21	178	12.6%	0.71 [0.34, 1.47]
Shah 2011	1	47	2	42	1.1%	0.43 [0.04, 4.98]
Thompson 2017	88	311	249	622	77.2%	0.59 [0.44, 0.79]
van Nunen 2016	11	20	14	15	1.4%	0.09 [0.01, 0.80]
Total (95% CI)		**749**		**1123**	**100.0%**	**0.58 [0.45, 0.75]**
Total events	122		298			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.49$, df = 5 (P = 0.63); $I^2 = 0\%$
Test for overall effect: Z = 4.16 (P < 0.0001)

A

Study or Subgroup	Minimally invasive Events	Minimally invasive Total	Open Events	Open Total	Weight	Odds Ratio M-H, Random, 95% CI
Arts 2018	4	121	4	66	24.8%	0.53 [0.13, 2.19]
Garber 2017	1	100	14	200	12.0%	0.13 [0.02, 1.04]
Han 2016	7	150	20	178	63.2%	0.39 [0.16, 0.94]
Total (95% CI)		**371**		**444**	**100.0%**	**0.37 [0.18, 0.75]**
Total events	12		38			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.27$, df = 2 (P = 0.53); $I^2 = 0\%$
Test for overall effect: Z = 2.77 (P = 0.006)

B

Study or Subgroup	Minimally invasive Events	Minimally invasive Total	Open Events	Open Total	Weight	Risk Ratio M-H, Random, 95% CI
Vogel 2014	2	21	21	21	9.5%	0.12 [0.04, 0.37]
Abbott 2012	3	10	9	10	11.0%	0.33 [0.13, 0.88]
Keshavarzi 2009	10	16	12	17	14.8%	0.89 [0.54, 1.44]
Arts 2018	26	121	66	66	15.7%	0.22 [0.16, 0.31]
Chan 2013	26	36	18	21	16.1%	0.84 [0.64, 1.10]
Thompson 2017	65	311	504	622	16.3%	0.26 [0.21, 0.32]
Han 2016	83	150	153	178	16.5%	0.64 [0.55, 0.75]
Total (95% CI)		**665**		**935**	**100.0%**	**0.40 [0.23, 0.70]**
Total events	215		783			

Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 121.97$, df = 6 (P < 0.00001); $I^2 = 95\%$
Test for overall effect: Z = 3.22 (P = 0.001)

C

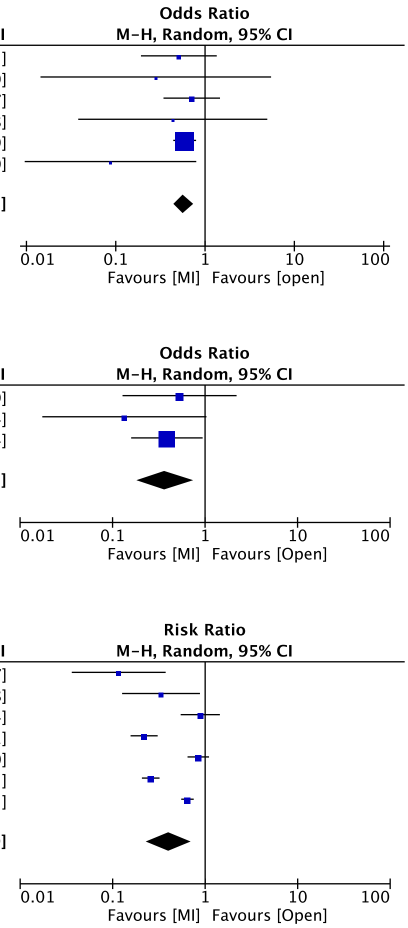


Fig. 3 Forest plots comparing **a** complications **b** reoperations, and **c** blood transfusion rate between open and minimally invasive craniosynostosis correction. MI minimally invasive

calvarial reconstruction, modified pi repair, etc. Thus, collectively, the current data in the literature remains weak. Nonetheless, strict adherence to the selection criteria, assessment for heterogeneity and subsequent use of remodeling when implicated, exclusion of single-arm case series, and thorough quality assessment with the GRADE tool allows us to provide the most valid comparison within the literature possible to date.

Directions for future investigations

While randomized comparisons would be ideal, but since they are harder to obtain, propensity-matched studies could be a useful alternative to account for age differences between patients undergoing either technique. Despite encouraging early results with anthropometric evaluations, more studies comparing such outcomes between the two techniques with a sufficient duration of follow-up are needed. More studies are also needed to evaluate outcomes following corrections for different types of craniosynostosis, since most of the literature at present is focused on the sagittal type. A longer duration of follow-up evaluation is required with endoscopic surgery to better assess its long-term complication and reoperation profile and allow a fair comparison with open reconstruction. Challenges associated with postoperative orthotic use also need to be investigated. Cost-directed investigations from varied practice settings would also welcome additions to the literature. At present, evidence for efficacy of endoscopic repair is largely available for nonsyndromic variants of craniosynostosis [2], obviating further studies comparing the two types of procedures for syndromic cases as well. Efforts must also be made to identify if there is a learning curve associated with the technique, although none yet has been acknowledged so far [2].

Conclusion

Early correction of craniosynostosis with minimally invasive endoscopic-assisted techniques might be associated with

Table 3 GRADE Summary of findings table (https://gradepro.org/)

Certainty assessment							No. of patients		Effect		Certainty
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MIS	Open craniosynostosis	Relative (95% CI)	Absolute (95% CI)	
Estimated blood loss											
8	Observational studies	Serious	Very serious	Not serious	Serious	Very strong association	494	547	–	MD 162.4 lower (245.51 lower to 79.28 lower)	⊕○○○ Very low
Length of stay											
9	Observational studies	Serious	Very serious	Not serious	Not serious	Strong association	711	1126	–	MD 2.56 lower (3.23 lower to 1.89 lower)	⊕○○○ Very low
Operative time											
9	Observational studies	Serious	Very serious	Not serious	Serious	Very strong association	689	1123	–	MD 112.38 lower (136.12 lower to 88.64 lower)	⊕○○○ Very low
Complications											
6	Observational studies	Serious	Not serious	Not serious	Very serious	None	122/749 (16.3%)	298/1123 (26.5%)	OR 0.68 (0.57 to 0.80)	70 more per 1000 (from 150 more to 10 fewer)	⊕○○○ Very low
Reoperations											
3	Observational studies	Serious	Very serious	Not serious	Very serious	None	12/371 (3.2%)	38/444 (8.6%)	OR 0.39 (0.20 to 0.77)	50 fewer per 1000 (from 18 fewer to 67 fewer)	⊕○○○ Very low
Transfusion rate											
7	Observational studies	Serious	Very serious	Not serious	Not serious	None	215/665 (32.3%)	783/935 (83.7%)	OR 0.40 (0.23 to 0.70)	164 fewer per 1000 (from 55 fewer to 295 fewer)	⊕○○○ Very low

CI confidence interval, *MD* mean difference, *OR* odds ratio lower perioperative morbidity, transfusion rate, and costs and non-inferior long-term improvement in cranial indices as compared to open surgery. These findings emphasize the need for early referral to a comprehensive craniofacial center in suspected cases of craniosynostosis as perioperative outcomes may be most optimized. Further prospectively randomized or propensity-matched comparisons with adequate duration of follow-up are required to validate these findings and elucidate the role of endoscopic surgery in craniosynostosis correction.

Compliance with ethical standards

Conflict of interest No funding sources or conflicts of interest to disclose.

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